

A4 - A NOVEL PEPTIDE ANTIBIOTIC ID: 4006

Featured Innovators: Y. Peter Di, PhD MBA and Berthony Deslouches, MD PhD

Infections that are resistant to antibiotics are a leading cause of death. The Centers for Disease Control reports that each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics. At least 23,000 people die each year as a direct result of these infections. The emergence of “superbugs” – bacteria resistant to all currently available antibiotics – are pushing us toward a “post-antibiotic era” where common infections would be untreatable. A4-antimicrobial peptides (A4-AMPs) are a new class of peptide-based antibiotic that kills more than 90% of antibiotic-resistant species of bacteria. Unlike antibiotics in current use, or in clinical development, A4 has a novel mechanism-of-action that does not confer resistance easily. A4 is a potential life-saving discovery that could be a key new weapon in the on-going battle with antibiotic-resistant bacteria.

Technology Description

A4 is an antimicrobial peptide-based antibiotics that target emerging antibiotic resistance. In both *in vitro* and *in vivo* preclinical testing, A4 has shown broad-spectrum bactericidal activity against a number of both gram-positive and gram-negative bacteria. A4 has the potential to become the next generation of potent antimicrobial agents to combat common, but dangerous (especially multiple drug resistant; MDR) bacterial infections.

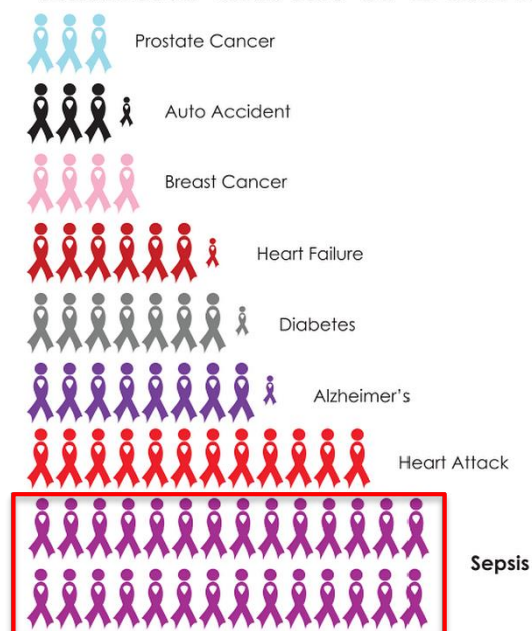
Advantages

- First new class of antibiotics in over the last 30 years
- Novel mechanism of action is expected to still possess strong efficacy against infections.
- A4-AMPs is in a fast-developing peptide-based antibiotic market that currently has limited competitors.

Applications

- Sepsis
- Respiratory tract infections
- Bacterial meningitis
- Endocarditis
- Urinary tract infections
- Skin infections
- Other MDR conditions

LEADING CAUSES OF DEATH



Stage of Development

Screening experiments *in vitro* have validated the excellent safety profile, the low propensity for drug resistance, and the strong antimicrobial activity of A4-AMPs against various superbugs. A selected lead compound of A4-AMPs was also successfully tested *in vivo* using mice, fully validating its safety and efficacy. Given the strategic need for new antimicrobials, clinical trials would likely be FDA fast-tracked when the IND is filed, and breakthrough status would be conferred upon a successful Phase 2 clinical trial.

IP Status

A provisional patent application was filed in 2016.

Innovators



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Dr. Di is a leading expert in airway epithelial pathobiology and immunity. His research has been continuously funded through various multi-year research awards including American Heart Association (AHA), Cystic Fibrosis Foundation (CFF), Flight Attendant Medical Research Institute (FAMRI), National Institute of Environmental Health Sciences (NIEHS), and National Heart, Lung and Blood Institute (NHLBI). Dr. Di actively collaborate with industry sponsors to perform pre-clinical testing and new drug development for MDR bacterial infection and cancer therapy.

Education

MBA University of California at Davis
PhD SUNY at Buffalo
BS Chung-Shan Medical and Dental College

Publications

- Sayeed S, Nistico L, St Croix C, Di YP. Multifunctional role of human SPLUNC1 in Pseudomonas aeruginosa infection. *Infection and immunity*. 2013;81(1):285-91.
- Liu Y, Bartlett JA, Di ME, Bomberger JM, Chan YR, Gakhar L, Mallampalli RK, McCray PB, Di YP. SPLUNC1/BPIFA1 contributes to pulmonary host defense against Klebsiella pneumoniae respiratory infection. *The American journal of pathology*. 2013;182(5):1519-31.
- Di YP, Tkach AV, Yanamala N, Stanley S, Gao S, Shurin MR, Kisin ER, Kagan VE, Shvedova A. Dual acute pro-inflammatory and anti-fibrotic pulmonary effects of SPLUNC1 after exposure to carbon nanotubes. *Am J Respir Cell Mol Biol*. 2013;49(5):759-67.
- Liu Y, Di ME, Chu HW, Liu X, Wang L, Wenzel S, Di YP. Increased susceptibility to pulmonary Pseudomonas infection in Splunc1 knockout mice. *The Journal of Immunology*. 2013;191(8):4259-68.



Berthony Deslouches, MD PhD

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Dr. Deslouches's research is directed toward the development of peptide-based antimicrobial therapeutics. In particular, he focuses on establishing a rational framework for guiding the optimization of peptide engineering for the property to overcome antibiotic resistance.

Education

MD/PhD University of Pittsburgh
MA City College of NY
BS City College of NY

Publications

- Deslouches B, Hasek ML, Craigo JK, Steckbeck JD, Montelaro RC. Comparative functional properties of engineered cationic antimicrobial peptides consisting exclusively of tryptophan and either lysine or arginine. *Journal of medical microbiology*. 2016 Jun 1;65(6):554-65.
- Deslouches B, Steckbeck JD, Craigo JK, Doi Y, Burns JL, Montelaro RC. Engineered cationic antimicrobial peptides to overcome multidrug resistance by ESKAPE pathogens. *Antimicrobial agents and chemotherapy*. 2015 Feb 1;59(2):1329-33.
- Deslouches B, Steckbeck JD, Craigo JK, Doi Y, Mietzner TA, Montelaro RC. Rational design of engineered cationic antimicrobial peptides consisting exclusively of arginine and tryptophan, and their activity against multidrug-resistant pathogens. *Antimicrobial agents and chemotherapy*. 2013 Jun 1;57(6):2511-21.
- Deslouches B, Gonzalez IA, DeAlmeida D, Islam K, Steele C, Montelaro RC, Mietzner TA. De novo-derived cationic antimicrobial peptide activity in a murine model of Pseudomonas aeruginosa bacteraemia. *Journal of antimicrobial chemotherapy*. 2007 Jul 10;60(3):669-72.

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